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L2: Entry 55 of 78 File: USPT Aug 24, 1999

US-PAT-NO: 5942437
DOCUMENT-IDENTIFIER: US 5942437 A

TITLE: Method and media for enhancing viability maturation, and cryopreservation of cells

DATE-ISSUED: August 24, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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US-CL-CURRENT: 435/374; 424/93.7, 435/1.3, 435/325, 435/347

L2: Entry 52 of 78 File: USPT Oct 26, 1999

DOCUMENT-IDENTIFIER: US 5972707 A
TITLE: Gene delivery system

Detailed Description Paragraph Right (11):
In general, the range of possible targets is dependent on the route of injection, e.g., intravenous or intraarterial, subcutaneous, intra-peritoneal, intrathecal, etc. For systemic injections, the specificity of this delivery system is affected by the accessibility of the target to blood borne nanospheres, which in turn, is affected by the size range of the particles. Size of the particles is affected by temperature, component concentration, and pH in the coacervation mixture. The particles can also be size-fractionated, e.g., by sucrose gradient ultracentrifugation. Particles with size less than 150 nanometers can access the interstitial space by traversing through the fenestrations that line most blood vessels walls. Under such circumstances, the range of cells that can be targeted is extensive. An abbreviated list of cells that can be targeted includes the parenchymal cells of the liver sinusoids, the fibroblasts of the connective tissues, the cells in the Islets of Langerhans in the pancreas, the cardiac myocytes, the Chief and parietal cells of the intestine, osteocytes and chondrocytes in the bone, keratinocytes, nerve cells of the peripheral nervous system, epithelial cells of the kidney and lung, Sertoli cells of the testis, etc. The targets for particles with sizes greater than 0.2 microns will be confined largely to the vascular compartment. Here, the targetable cell types include erythrocytes, leukocytes (i.e. monocytes, macrophages, B and T lymphocytes, neutrophils, natural killer cells, progenitor cells, mast cells, eosinophils), platelets, and endothelial cells.

Detailed Description Paragraph Right (12):
For subcutaneous injections, the targetable cells include all cells that resides in the connective tissue (e.g., fibroblasts, mast cells, etc.), Langerhans cells, keratinocytes, and muscle cells. For intrathecal injections, the targetable cells include neurons, glial cells, astrocytes, and blood-brain barrier endothelial cells. For intraperitoneal injection, the targetable cells include the macrophages and neutrophils.

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L2: Entry 40 of 78 File: USPT Jan 2, 2001

DOCUMENT-IDENTIFIER: US 6169070 B1
TITLE: Mer receptor activation by gas6

Brief Summary Paragraph Right (2):
The invention relates generally to methods of activating the Rse or Mer tyrosine kinase receptors. More particularly, the invention relates to methods of enhancing survival, proliferation and/or differentiation of cells comprising the Rse receptor (such as glial cells) or Mer receptor (e.g. monocytes) using gas6. The invention also relates to gas6 variants, particularly those which are less .gamma.-carboxylated than gas6 isolated from nature.

Brief Summary Paragraph Right (14):
The invention further provides a method of activating Rse or Mer receptor by exposing a cell (preferably a human cell) comprising the Rse or Mer receptor to exogenous gas6 in an amount effective to activate the Rse or Mer receptor. The Rse or Mer receptor is normally cell-bound and the gas6 is preferably human gas6. The invention also provides a method of enhancing survival, proliferation and/or differentiation of a cell which has the Rse or Mer receptor incorporated in the cell membrane thereof by exposing the cell to gas6 in an amount effective to enhance survival, proliferation and/or differentiation of the cell. The cell may be a neuron or a glial cell, such as a Schwann cell, or a monocyte (e.g. a macrophage). The cell may be present in cell culture or in a mammal (e.g. a human) which is suffering from a neurologic disease or disorder. Often, the gas6 is provided in a physiologically acceptable carrier.

Detailed Description Paragraph Right (4):
A gas6 variant is included within the scope of the invention provided that it is functionally active. As used herein, "functionally active" and "functional activity" in reference to gas6 means that the gas6 is able to activate the Rse receptor and/or Mer receptor and/or promote the proliferation, survival, and/or differentiation of cells comprising the Rse receptor or Mer receptor such as neurons, glial cells or monocytic cells. A "glial cell" is derived from the central and peripheral nervous system and can be selected from oligodendroglial, astrocyte, ependymal, or microglial cells as well as satellite cells of ganglia and the neurolemmal or Schwann cells around peripheral nerve fibers. A "monocytic cell" is a mononuclear leukocyte such as a macrophage.

Detailed Description Paragraph Right (109):
Propagation of vertebrate cells in culture (tissue culture) has become a routine procedure in recent years (Tissue Culture, Academic Press, Kruse and Patterson, editors [1973]). Examples of useful mammalian host cell lines are monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., J. Gen Virol. 36:59 [1977]); baby hamster kidney cells (BHK, ATCC CCL 10); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. Sci. USA 77:4216 [1980]); mouse sertoli cells (TM4, Mather, Biol. Reprod. 23:243-251 1980]); monkey kidney cells (CV1 ATCC CCL 70); African green monkey kidney cells (VERO-76, ATCC CRL-1587); human cervical carcinoma cells (HELA, ATCC CCL 2); canine kidney cells (MDCK, ATCC CCL 34); buffalo rat liver cells (BRL 3A, ATCC CRL 1442); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); mouse mammary tumor (MMT 060562, ATCC CCL51); TRI cells (Mather et al., Annals N.Y. Acad. Sci. 383:44-68 [1982]); MRC 5 cells; FS4 cells; and a human hepatoma line (Hep G2).

Detailed Description Paragraph Right (122):
In accordance with the in vitro methods of the invention, cells comprising the Rse or Mer receptor are provided and placed in a cell culture medium. Examples of Rse-receptor-containing cells include neural cells, e.g., brain cells (such as neurons

of the neocortex, cerebellum and hippocampus); glial cells (e.g. Schwann cells or astrocytes); kidney or breast-derived cells; cells derived from the ovary or testes; fibroblast cells such as mouse 3T3 cells; cells from the hematopoietic system such as CMK11-5. Examples of Mer-receptor-containing cells include peripheral blood mononuclear cells, bone marrow mononuclear cells. monocytes, primary hematopoietic cells and cells derived from testis, ovary, prostate, lung, kidney, spleen, peripheral blood leukocyte, placenta, thymus, small intestine, colon or liver. Exemplary cell lines to be cultured using gas6 include T lymphocyte leukemia cell lines (e.g. CCRF-HSB-2, JURKAT, HPB-ALL and Peer); K-562 cell line; monocytic leukemia/lymphoma cell lines (such as U-937); megakaryoblastic leukemia cell lines (e.g. UT-7) and other cell lines which express Mer receptor as described in Graham et al., Cell Growth Differ. 5:647 (1994).

Detailed Description Paragraph Right (127):
The invention also provides in vivo uses for gas6. Based on the ability of gas6 to promote proliferation of glial cells (see Example 9), it is believed that this molecule will be particularly useful for treating diseases which involve demyelination, damage or loss of glial cells (e.g. multiple sclerosis).

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L2: Entry 38 of 78 File: USPT Mar 13, 2001

DOCUMENT-IDENTIFIER: US 6200780 B1
TITLE: Human interferon-.epsilon.(IFN-.epsilon.), a type I interferon

Detailed Description Paragraph Right (86):
Suitable host cells for the expression of glycosylated IFN-.epsilon. are derived from multicellular organisms. Examples of invertebrate cells include insect cells such as Drosophila S2 and Spodoptera Sf9, as well as plant cells. Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells. More specific examples include monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., J. Gen Virol., 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. Sci. USA, 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod., 23:243-251 (1980)); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); and mouse mammary tumor (MMT 060562, ATCC CCL51). The selection of the appropriate host cell is deemed to be within the skill in the art.

Detailed Description Paragraph Right (168):
Exemplary conditions or disorders to be treated include benign or malignant tumors (e.g. renal, liver, kidney, bladder, breast, gastric, ovarian, colorectal, prostate, pancreatic, lung, vulval, thyroid, hepatic carcinomas; sarcomas; glioblastomas; and various head and neck tumors); leukemias and lymphoid malignancies; other disorders such as neuronal, glial, astrocytal, hypothalamic and other glandular, macrophagal, epithelial, stromal and blastocoelic disorders; and inflammatory, angiogenic and immunologic disorders.